

What is claimed is:

1. A small interfering RNA (siRNA) comprising a sequence sufficiently complementary to a portion of the HIV genome to mediate RNA interference (RNAi).

5

2. The siRNA of claim 1, wherein the siRNA is between about 15 and about 25 nucleotides long.

3. The siRNA of claim 1, wherein the siRNA is between about 20 and about 23
10 nucleotides long.

4. The siRNA of claim 1, wherein the siRNA comprises a sequence sufficiently complementary to a Long Terminal Repeats (LTR) region of the HIV genome to mediate RNAi.

15 5. The siRNA of claim 1, wherein the siRNA comprises a sequence sufficiently complementary to a *nef* gene of the HIV genome to mediate RNAi.

6. The siRNA of claim 1, wherein the siRNA comprises a sequence sufficiently complementary to a *vif* gene of the HIV genome to mediate RNAi.

20

7. The siRNA of claim 1, wherein the siRNA comprises a sequence sufficiently complementary to a gene of the HIV genome that codes for a reverse transcriptase enzyme to mediate RNAi.

25 8. The siRNA of claim 1, wherein the siRNA comprises a sequence sufficiently complementary to a gene of the HIV genome that codes for a capsid protein or an envelope protein to mediate RNAi.

9. The siRNA of claim 1, wherein the siRNA is an expressed siRNA.

30

10. The siRNA of claim 1, wherein the siRNA is a synthetic siRNA.

11. The siRNA of claim 10, wherein the siRNA is a synthetic 21-nucleotide siRNA.

12. The siRNA of claim 1, wherein the siRNA is a short hairpin siRNA (shRNA).

5 13. The siRNA of claim 1, wherein the siRNA is a short hairpin siRNA (shRNA) expressed from a plasmid.

14. The siRNA of claim 1, wherein the siRNA inhibits synthesis of viral HIV cDNA.

10 15. The siRNA of claim 1, wherein the siRNA promotes the degradation of or inhibits synthesis of viral HIV cDNA intermediates.

16. The siRNA of claim 1, wherein the siRNA promotes the degradation of or inhibits synthesis of genomic viral HIV RNA.

15 17. The siRNA of claim 1, wherein the siRNA mediates RNAi during an early viral replication cycle event.

20 18. The siRNA of claim 1, wherein the siRNA mediates RNAi during a late viral replication cycle event.

19. The siRNA of claim 1, wherein the siRNA is generated by endonuclease cleavage of dsRNA.

25 20. The siRNA of claim 1, wherein the siRNA is modified by the substitution of at least one nucleotide with a modified nucleotide.

21. The siRNA of claim 1, wherein the siRNA has at least one mismatch when compared to the sequence of the HIV genome.

30

22. A siRNA complex comprising:
the siRNA of claim 1; and
one or more proteins associated with the siRNA that recognize the portion of the HIV
genome.

5

23. A method of treating a subject infected with HIV, the method comprising the
steps of:

providing an siRNA comprising a sequence sufficiently complementary to a portion of
the HIV genome to mediate RNA interference (RNAi); and

10 initiating RNAi by administering the siRNA to said subject.

24. The method of claim 23, comprising the step of providing a siRNA complex
comprising:

15 the siRNA comprising a sequence sufficiently complementary to a portion of the HIV
genome to mediate RNA interference (RNAi); and

one or more proteins associated with the siRNA that recognize the portion of the HIV
genome.

25 25. The method of claim 23 comprising the step of providing a siRNA complex
20 comprising the siRNA.

26. The method of claim 23 comprising the steps of:

analyzing a portion of an HIV genome present in the subject; and

25 providing an siRNA comprising a sequence sufficiently complementary to the portion of
the HIV genome present in the subject to mediate RNAi.

27. The method of claim 23 comprising the steps of:

analyzing a portion of an HIV genome, for each of a plurality of mutated HIV genomes
present in the subject; and

30 providing one or more siRNAs comprising a sequence sufficiently complementary to the
portion of the HIV genome, for each of the plurality of mutated HIV genomes present in the
subject.

28. A method of inhibiting or preventing HIV replication or infection in a subject, the method comprising the steps of:

providing a siRNA comprising a sequence sufficiently complementary to a portion of the
5 HIV genome to mediate RNA interference (RNAi); and
administering the siRNA to the subject the siRNA such that HIV replication or infection is inhibited or prevented.

29. The method of claim 28 wherein the siRNA is expressed from a vector template.

30. The method of claim 28, wherein viral RNA is degraded in the early stages of replication such that provirus formation is inhibited or prevented.

31. The method of claim 28, wherein viral RNA is degraded in the late stages of
15 replication such that release of newly formed viral RNA is inhibited or prevented.

32. The method of claim 28 comprising the steps of:
analyzing a portion of an HIV genome present in the subject; and
providing an siRNA comprising a sequence sufficiently complementary to the portion of
20 the HIV genome present in the subject to mediate RNAi.

33. The method of claim 28 comprising the steps of:
analyzing a portion of an HIV genome, for each of a plurality of mutated HIV genomes present in the subject; and
25 providing one or more siRNAs comprising a sequence sufficiently complementary to the portion of the HIV genome, for each of the plurality of mutated HIV genomes present in the subject.

34. A method of inhibiting or preventing HIV replication or infection in a cell, the
30 method comprising the steps of:
providing a siRNA comprising a sequence sufficiently complementary to a portion of the HIV genome to mediate RNA interference (RNAi); and

inhibiting or preventing HIV replication or infection by contacting a cell with the siRNA.

35. The method of claim 34, wherein the siRNA is expressed from a vector.

5 36. The method of claim 34, wherein viral RNA is degraded in the early stages of replication such that provirus formation is inhibited or prevented.

37. The method of claim 34, wherein viral RNA is degraded in the late stages of replication such that release of newly formed viral RNA from the cell is inhibited or prevented.

10 38. The method of claim 34, comprising the step of providing a cell unexposed to the HIV virus.

39. The method of claim 34, comprising the step of providing a cell comprising less
15 than 500 copies of viral HIV RNA.

40. The method of claim 34, comprising the step of providing a cell comprising less than 1000 copies of viral HIV RNA prior to contacting the cell with the siRNA.

20 41. The method of claim 34, comprising the step of providing a cell exposed to HIV, but wherein the HIV RNA has not integrated into the cell genome.

42. The method of claim 34, wherein said cell is a lymphocyte.

25 43. The method of claim 42, wherein said lymphocyte is a primary peripheral blood lymphocyte.

44. The method of claim 34, wherein the siRNA is expressed from a vector template
in vivo.

30 45. A vector that expresses an siRNA comprising a sequence sufficiently complementary to a portion of the HIV genome to mediate RNA interference (RNAi).

46. The vector of claim 45, wherein the siRNA is a shRNA.

47. The vector of claim 45 wherein the vector expresses a plurality of siRNAs
5 comprising sequences sufficiently complementary to portions of the HIV genome to mediate
RNAi.

48. The vector of claim 47 wherein at least one of the siRNAs is a shRNA.

49. The vector of claim 47 wherein the plurality of siRNAs comprise sequences
10 sufficiently complementary to staggered portions of the HIV genome to mediate RNAi.

50. The vector of claim 47 wherein the plurality of siRNAs comprise sequences
sufficiently complementary to different genes in the HIV genome.

51. The vector of claim 47 wherein the plurality of siRNAs comprise at least three
15 sequences sufficiently complementary to one or more regions of the HIV genome selected from
the group consisting of: a region coding for reverse transcriptase, a region coding for protease,
and a *vif* gene.

52. The vector of claim 47 wherein the plurality of siRNAs comprise at least five
20 sequences sufficiently complementary to one or more regions of the HIV genome selected from
the group consisting of: a region coding for reverse transcriptase, a region coding for protease, a
tat gene, a *rev* gene, and a *vif* gene.

53. The vector of claim 47 wherein the plurality of siRNAs comprise sequences
25 sufficiently complementary to one or more regions of the HIV genome selected from the group
consisting of: a region coding for reverse transcriptase, a region coding for protease, a *tat* gene, a
rev gene, and a *vif* gene, a *gag* gene, a *vpr* gene, a region coding for an envelope protein, a region
coding for a capsid protein, and a LTR region.

54. The vector of claim 47 wherein the vector is a plasmid vector.
30

55. The vector of claim 47 wherein the vector is a viral vector.

56. A method of treating a subject infected with HIV, the method comprising the steps of:

5 providing the vector of claim 45; and
initiating RNA interference by administering the vector to said subject.

57. The method of claim 56, wherein viral RNA is degraded in the early stages of replication such that provirus formation is inhibited or prevented.

10 58. The method of claim 56, wherein viral RNA is degraded in the late stages of replication such that release of newly formed viral RNA is inhibited or prevented.

59. The method of claim 56 comprising the steps of:
15 analyzing a portion of an HIV genome present in the subject; and
providing an siRNA comprising a sequence sufficiently complementary to the portion of the HIV genome present in the subject to mediate RNAi.

60. The method of claim 56 comprising the steps of:
20 analyzing a portion of an HIV genome, for each of a plurality of mutated HIV genomes present in the subject; and
providing one or more siRNAs comprising a sequence sufficiently complementary to the portion of the HIV genome, for each of the plurality of mutated HIV genomes present in the subject.

25 61. A method of inhibiting or preventing HIV replication or infection in a subject, the method comprising the steps of:

providing the vector of claim 45; and
initiating RNA interference by administering the vector to said subject.

30 62. The method of claim 61, wherein viral RNA is degraded in the early stages of replication such that provirus formation is inhibited or prevented.

63. The method of claim 61, wherein viral RNA is degraded in the late stages of replication such that release of newly formed viral RNA is inhibited or prevented.

5 64. The method of claim 61 comprising the steps of:
analyzing a portion of an HIV genome present in the subject; and
providing an siRNA comprising a sequence sufficiently complementary to the portion of the HIV genome present in the subject to mediate RNAi.

10 65. The method of claim 61 comprising the steps of:
analyzing a portion of an HIV genome, for each of a plurality of mutated HIV genomes present in the subject; and
providing one or more siRNAs comprising a sequence sufficiently complementary to the portion of the HIV genome, for each of the plurality of mutated HIV genomes present in the
15 subject.

66. A method of inhibiting or preventing HIV replication or infection in a cell, the method comprising the steps of:
providing the vector of claim 45; and
20 initiating RNA interference by administering the vector to said cell.

67. The method of claim 66, wherein viral RNA is degraded in the early stages of replication such that provirus formation is inhibited or prevented.

25 68. The method of claim 66, wherein viral RNA is degraded in the late stages of replication such that release of newly formed viral RNA from the cell is inhibited or prevented.

69. The method of claim 66, comprising the step of providing a cell unexposed to the HIV virus.

30 70. The method of claim 66, comprising the step of providing a cell comprising less than 500 copies of viral HIV RNA.

71. The method of claim 66, comprising the step of providing a cell comprising less than 1000 copies of viral HIV RNA prior to contacting the cell with the siRNA.

5 72. The method of claim 66, comprising the step of providing a cell exposed to HIV, but wherein the HIV RNA has not integrated into the cell genome.

73. The method of claim 66, wherein said cell is a lymphocyte.

10 74. The method of claim 73, wherein said lymphocyte is a primary peripheral blood lymphocyte.